

# **Exhibit 21**

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# ATTENDEES

**National Immunotherapy Initiative**

December 1, 2015

## HOST



**Vice President Joe Biden**

47<sup>th</sup> Vice President of the United States  
White House

## ATTENDEES

### WHITE HOUSE



**Don Graves**

White House  
Deputy Assistant to the President and Counselor to the Vice President

### FDA



**Robert M. Califf, M.D.**

U.S. Food and Drug Administration  
Deputy Commissioner for Medical Products and Tobacco



**Janet Woodcock, M.D.**

U.S. Food and Drug Administration  
Director of the Center for Drug Evaluation and Research (CDER)



**Peter W. Marks, M.D., Ph.D.**

U.S. Food and Drug Administration  
Deputy Director for the Center for Biologics Evaluation and Research (CBER)

### NCI



**Jeffrey Schlom, Ph.D.**

Center for Cancer Research, National Cancer Institute, National Institutes of Health  
Chief - Laboratory of Tumor Immunology and Biology



**James L. Gulley M.D., Ph.D., F.A.C.P.**

Center for Cancer Research, National Cancer Institute, National Institutes of Health  
Head - Immunotherapy Section, Chief - Genitourinary Malignancies Branch,  
Director - Medical Oncology Service

## ATTENDEES

### CLINICAL LEADERSHIP



**Andrew M. Evens, D.O., MSc, F.A.C.P.**

Tufts University School of Medicine

Professor & Chief, Division of Hematology/Oncology, Director of Tufts Cancer Center



**Ralph H. Hruban, M.D.**

Johns Hopkins University

Professor of Pathology & Oncology at Johns Hopkins University School of Medicine

Director of The Sol Goldman Pancreatic Cancer Research Center



**Vivian S. Lee, M.D., Ph.D., M.B.A.,**

University of Utah Senior Vice President for Health Sciences

Dean of the School of Medicine

CEO, University of Utah Health Care



**Stephen D. Nimer, M.D.**

University of Miami Health System

Director, Sylvester Comprehensive Cancer Center Professor of Medicine,  
Biochemistry & Molecular Biology and Professor of Medicine



**Mark C. Poznansky, M.D., Ph.D.**

Harvard Medical School

Director - Vaccine & Immunotherapy Center

Harvard Medical School, Physician at Massachusetts General Hospital



**Azra Raza, M.D.**

Columbia University

Director of the MDS Center, Professor of Medicine



**Col. Craig Shriver, M.D., F.A.C.S.**

Walter Reed National Military Medical Center

Colonel, Medical Corps, United States Army

Director, John P. Murtha Cancer Center



**Patrick Soon-Shiong, M.D., F.R.C.S.(C), F.A.C.S.**

NantWorks & Chan Soon-Shiong Institute of Molecular Medicine (CSSIOM)

Founder & Chairman

## ATTENDEES

### PHARMA



**Robert A. Bradway**

Amgen  
Chairman & Chief Executive Officer



**Paul Seligman, M.D., M.P.H.**

Amgen  
Chief of R&D Policy



**Sir Andrew Witty**

GlaxoSmithKline  
Chief Executive Officer



**Patrick Vallance**

GlaxoSmithKline  
President, Pharmaceuticals Research & Development



**Mikael Dolsten, M.D., Ph.D.**

Pfizer  
President, Worldwide Research & Development



**Frank Jones, M.D.**

Etubics Corporation  
President, Chief Executive Officer, Chief Scientific Officer

### PAYORS & INTEROPERABILITY



**Jim Huffman**

Bank of America  
Senior Vice President, Head of U.S. Health and Wellness Benefits



**Daniel J. Hilferty**

Independence Blue Cross  
President and Chief Executive Officer



**Paul M. Black**

Allscripts  
Chief Executive Officer & Director



**John Chen**

Blackberry  
Executive Chairman & Chief Executive Officer

# **Exhibit 22**

# **Exhibit 22**



**HISTORIC NATIONAL COALITION FORMED TO ACCELERATE NEXT GENERATION  
IMMUNOTHERAPY IN CANCER**

**LARGE PHARMA, BIOTECH, MAJOR PAYER, FORTUNE 50 COMPANY, ACADEMIA AND  
COMMUNITY ONCOLOGISTS JOIN FORCES TO ANNOUNCE LAUNCH OF CANCER MOONSHOT  
2020 PROGRAM**

- **Nation's first insurance coverage of next generation whole genome sequencing and proteomic diagnostic platform in cancer patients**
- **Next generation sequencing and precision medicine evolving from research to the clinical trial and cancer care setting**
- **Coalition to design, initiate and complete randomized clinical trials at all stages of cancer in up to 20 tumor types in as many as 20,000 patients in multiple phase 1 to 3 trials by year 2020**
- **Beneficiaries and patients will undergo next-generation molecular sequencing and gain access to over 60 novel and approved molecules to be tested as immunotherapy combinations in 20,000 cancer patients with cancer across all tumor types: The QUILT Program**

**SAN FRANCISCO – January 11, 2016** – Today, leaders from large pharma including Celgene and Amgen, biotech including NantWorks, NantKwest, Etubics, Altor Bioscience, and Precision Biologics, major academic cancer centers and community oncologists announced the launch of [\*\*The National Immunotherapy Coalition \(NIC\)\*\*](#), a historic alliance--in collaboration with Independence Blue Cross, one of the nation's largest payers and Bank of America, one of the largest self-insured companies in the U.S.--with a singular focus: accelerating the potential of combination immunotherapies as the next generation standard of care in patients with cancer.

This unprecedented collaboration of multinational pharmaceutical, biotechnology companies, academic centers and community oncologists will make possible access to over 60 novel and approved agents under exploration in the war against cancer and will enable rapid testing of novel immunotherapy combination protocols, forming the basis of [\*\*The Cancer MoonShot 2020\*\*](#) (<http://www.CancerMoonShot2020.org>). The NIC will design, initiate and complete randomized clinical trials in cancer patients with cancer at all stages of disease in up to 20 tumor types in as many as 20,000 patients by the year 2020.

### **The QUILT Program**

The QUILT (QUantitative Integrative Lifelong Trial) program is designed to harness and orchestrate all the elements of the immune system (including dendritic cell, T cell and NK cell therapies) by testing novel combinations of vaccines, cell-based immunotherapy, metronomic chemotherapy, low dose radiotherapy and immunomodulators -- including check point inhibitors-- in patients who have undergone next generation whole genome, transcriptome and quantitative proteomic analysis, with the goal of achieving durable, long-lasting remission for patients with cancer.

The multiple Phase 1 and 2 protocol designs will be a collaboration between academia, pharma, and clinical scientific experts in immunotherapy in accordance with the recent published U.S. Food and Drug Administration guidance of “Co-development of Two or More New Investigational Drugs for Use in Combination.” Multiple companies are currently exploring first-in-human clinical trials as part of agreements between government agencies, including Immunology Branches of NCI, academia and community oncologists. Multiple randomized Phase 2 trials testing genomically and proteomically informed novel combinations of immunotherapy agents, will pave the way to identifying cancer therapy combinations with the lowest toxicity and the highest quality of life.

Both academic cancer centers and community oncologists will participate in the QUILT Program to enroll 20,000 patients by 2020. The QUILT Program will be stratified across multiple Phase 1 and Phase 2 trials, addressing up to 20 tumor types including breast, lung, prostate, ovarian, brain, head and neck, multiple myeloma, sarcoma, pancreatic cancer, among others. Pharmaceutical and biotechnology partners have made an unprecedented commitment to make more than 60 novel immunotherapy, targeted therapy and chemotherapeutic agents available to be combined across multiple tumor types.

"There are unique times in history when events and advancements in technology converge to elicit a quantum leap in medical care. This is not only a unique time, but also a unique inflection point in the history of cancer," said Dr. Patrick Soon-Shiong, M.D., Founder and Chief Executive Officer of NantWorks and the Chan Soon-Shiong Institute of Molecular Medicine. "The era of immunotherapy has taken the oncology world by storm. For the first time in 40 years there is a glimmer that we may be able to win this war against cancer. Large pharma and biotech companies are developing dozens of agents to activate the immune system. The problem is that while these drugs are being developed individually in silos by each entity, they need to act together when it comes to activating the immune system. If we follow the current path of drug development, it may take 40 or 50 years before we have worked out the right cocktail combination and countless lives will be lost as a result of this inefficiency."

Dr. Soon-Shiong continued, "Our knowledge in the science of genomics, proteomics, immunology and immunotherapy has advanced and converged at an unprecedented speed, making now the time for the rapid deployment and orchestration of immunotherapy for the benefit of millions of cancer patients. The Cancer MoonShot 2020 Program, the National



Immunotherapy Coalition and the QUILT Program are designed to do just that, bring together a diverse group of visionary leaders and stakeholders to pool resources and bring to patients a dramatic improvement in cancer care."

### **Nation's First Insurance Coverage by Independence Blue Cross for Next Generation Panomic Sequencing Immunotherapy Moves Precision Medicine in Oncology from Bench to Bedside**

"The insurance coverage of whole genome transcriptomic tests in patients receiving immunotherapy by Independence Blue Cross is a landmark milestone in moving precision medicine in oncology from the bench to the bedside" Dr. Soon-Shiong stated "Independence Blue Cross has taken the visionary lead to cover next generation sequencing. We are in discussions with the rest of the insurance industry, including Blue Cross on a national basis to encourage the industry to follow Independence's lead."

"At Independence Blue Cross, we are proud to be the first major insurer offering reimbursement to our members for this next generation whole genome sequencing," said Daniel J. Hilferty, President and Chief Executive Officer of Independence of Health Group. "We are committed to bringing state-of-the-art advances in oncology care to our members and making care accessible and affordable."

### **Mission of Cancer MoonShot 2020 Program**

The mission of the Cancer MoonShot 2020 Program is to rapidly enroll and complete randomized Phase 2 clinical trials to validate the potential of panomic (whole genome, transcriptome and proteomic) analyses and to evaluate novel combination immunotherapies as the next generation standard of care. This coalition combines the efforts not only of major academic centers but also the community oncologists, enabling accelerated recruitment of patients to multiple Phase II trials. Utilizing a secure cloud-based infrastructure to integrate and enable the participation of both major academic and community oncologists at a national scale, the goal is to complete randomized clinical trials in patients with cancer at all stages of disease, across up to 20 tumor types in 20,000 patients within the next 36 months. By comparing standards of care to the next paradigm of less toxic immunotherapy combination therapy, the findings of these in the randomized QUILT Program will inform the design of Phase 3 registration trials, with the goal of bringing transformative advances in combination immunotherapies to cancer patients by 2020.

Col. Craig Shriver, M.D., FACS at the John P Murtha Cancer Center at Walter Reed Military Hospital and United States Army said, "We validate big science through our clinical trials network. There are 1.2 million active duty military members, 9.3 million beneficiaries that receive military health care. That's a huge network. Just in our active duty force, we get a thousand active duty members a year that come down with cancer. If a thousand active duty members were still getting injured in Afghanistan or Iraq, we would not accept this. So it's the same thing with how militaries respond to infectious diseases, illnesses that affect the readiness of our active force. Cancer is that threat."

### **Large Pharma and Biotech Collaboration**

In this historic collaboration, large pharmaceutical and biotechnology companies --NantWorks, NantKwest, Etubics, Precision Biologics, and Altor Bioscience—along with others, have agreed to contribute their novel immunotherapy molecules, including adenovirus vaccines, neoepitopes antibodies, and natural killer cells, to accelerate the development of next generation immunotherapy combination cancer therapies across all tumor types.

“I am pleased that visionary leaders in the healthcare industry have agreed to participate in the early formation and launch of this coalition. Several pharma companies, biotechnology companies and others are currently assessing the opportunity to join the coalition at this early stage. As the Cancer MoonShot 2020 program coalesces and demonstrates rapid enrollment of patients, I am hopeful that many more multinational pharma leaders in the immunotherapy space, as well as other leaders in biotech, will agree to join this collaboration to accelerate immunotherapy development for the benefit of cancer patients.” said Dr. Soon-Shiong.

Celgene has established a research center of excellence focused on immunotherapy approaches such as checkpoint inhibitors, CAR-T therapies, NK cells, stem cells and others. Celgene has also advanced new approaches to chemotherapy, including the development of Abraxane®, the first cancer nanotechnology therapy globally approved for the treatment of breast cancer, lung cancer and pancreatic cancer. Celgene will participate in the Cancer MoonShot 2020 Program by applying its deep and diverse library of important molecules, both approved and in the development pipeline, to the QUILT Program. Robert J. Hugin, Chairman and Chief Executive Officer, Celgene Corporation said: “At Celgene, we are fully committed to the Cancer MoonShot 2020 Program as a part of our longstanding efforts to discover and develop new therapies for difficult to treat cancers. We have learned that the research and development of breakthrough treatments for patients requires novel approaches, bold science and strong vision. To realize this vision, we are excited to participate in the Cancer MoonShot 2020 Program by applying our deep and diverse library of important molecules, both approved and in the development pipeline, to the QUILT Trials, which we believe will play an important role in the rapid advancement of immuno-oncology for patients with life-threatening cancers.”

Paul Seligman, M.D., MPH, Amgen, Chief of R&D Policy: “At AMGEN, we are committed to using genomics and deep insights into biology to develop novel therapies for cancer. We are committed to the goals of collaborative research efforts in immuno-oncology and the development of innovative combination therapies. It is a time of unprecedented progress in our ability to understand how to harness the power of the immune system to treat tumors, and collaborative approaches represent a tremendous opportunity to combine the efforts of key stakeholders to accelerate progress.”

Luciano Rossetti, M.D., Executive Vice President and Head of Global R&D for the biopharmaceutical business of Merck KGaA, Darmstadt, Germany: “In 2014, Merck KGaA, Darmstadt, Germany, and Pfizer formed a global strategic alliance to jointly develop immuno-

oncology compounds. Forging strong partnerships between academia and the healthcare industry is of strategic importance in sharing knowledge and more effectively addressing existing challenges in cancer care. We look forward to learning more about this initiative, as we share a common goal of improving patient outcomes through the combination of highly innovative novel-novel therapies in the field of immuno-oncology."

Frank R. Jones, Ph.D., Chairman, President, and Chief Executive Officer of Etubics Corporation: "At Etubics, we specialize in developing innovative immunotherapies and vaccines for a wide-range of resilient diseases including cancer, so it goes without saying that we are extremely excited about this new initiative. We recognize the value in an immune stimulation treatment approach and look forward to volunteering our agents for combination clinical trials that we anticipate will produce groundbreaking results."

Hing C. Wong, Ph.D., CEO and Founder of Altor Bioscience Corporation said, "We have focused our technology pipeline on cytokine-based immunotherapies. We have discovered exciting results when combining our immunostimulant molecules with other elements of the immune system, such as natural killer and T cells. The opportunity to accelerate development of our molecules in combination with other technologies in the field of immuno-oncology is a major step to advancing their clinical development. We have enthusiastically joined this coalition and are honored to been given this opportunity to play a part in the Cancer MoonShot 2020 program."

#### **Academic NCI – Designated Cancer Centers and Community Oncologists**

The successful accrual of 20,000 patients by 2020 will require both community oncologists and major medical centers to collaborate for the common good. The partnership also anticipates the participation of the military health system.

Tom Kurtz, CEO of Windber Medical Center and Windber Research Institute: "Walter Reed has had a long standing partnership with the Windber Research Institute and through our collaborative efforts, we were responsible for providing over 90% of the breast cancer tissue genetically analyzed by the NIH Cancer Genome Atlas study. This human tissue repository is the nation's foremost Platinum-rated, CLIA CAP certified bio-repository for cancer tissue housing over 90,000 tissue specimens, and will be utilized as the tissue repository resource to support the QUILT Program. We are proud to be involved in this historic national initiative and to expand the efforts to elucidate the biologic mysteries of cancer and build on our work in genomics over the last decade. Windber Medical Center is a small community hospital supporting a population of 4,000. Cancer is a major issue as our population ages. It is a major honor and opportunity for our community to participate and have access to cutting edge technology through this Cancer MoonShot 2020 program."

Michael M. Crow, President of Arizona State University said, "American higher education cannot assume that its competitive position in the world is unassailable. Our research

universities must innovate to survive, and this Cancer MoonShot 2020 Program is an opportunity to innovate in healthcare research and training for the benefit of humanity. This program will link scientists and technological advances across dozens of areas around a single goal: clinical treatments individualized to the disease in a particular person. ASU is proud to be partners with NantWorks and the Chan Soon-Shiong Institute of Molecular Medicine in the development of a campus in Phoenix where the next generation of scientists, clinical decision specialists, integrated precision medicine engineers and medical data analysts can be trained for both research and healthcare delivery."

Ralph H. Hruban, M.D., Professor of Pathology & Oncology at Johns Hopkins University School of Medicine and Director of The Sol Goldman Pancreatic Cancer Research Center: "We are at a crossroads, a time of discovery that's transforming the ways we manage cancer. Johns Hopkins researchers and clinicians are working tirelessly to understand cancer better and to move treatments from bench to bedside so that patients can have a better shot at beating the disease. It is my hope that the National Immunotherapy Coalition, and others like it, will advance the understanding of cancer, not by small steps, but instead by leaps and bounds."

Mark C. Poznansky, M.D., Ph. D. Director – Vaccine & Immunotherapy Center, Physician - Massachusetts General Hospital, Associate Professor, Harvard Medical School: "The time is now to create an accelerated path, and advance medical science forward to save lives and improve health worldwide. The National Immunotherapy Coalition clearly unites and leverages the resources and expertise of a diverse network of medical and business professionals to safely and rigorously accelerate the pace of discovery, development and actualization of cancer treatment. By accelerating the development of new safe and cost effective therapies combating cancer, we can bring them to those that are most in need faster and more cost effectively than current approaches."

Manuel Hidalgo, M.D., Ph. D. Chief, Division of Hematology/Oncology and Clinical Director, Cancer Center at Beth Israel Deaconess Medical Center, Harvard Medical School. "We are now glimpsing the potential of modulating the immune system to treat cancer in an effective way. Integrating multiple treatment strategies in innovative clinical trial protocols is the path to make a real impact in cancer care. In the Cancer Center at BIDMC, we are constantly working to discover and implement new treatments for our patients. We are very excited to work with The National Immunotherapy Coalition and join efforts to advance cancer medicine."

Azra Raza, M.D., Columbia University, Director of MDS Center, Professor of Medicine: "We are very pleased to have the opportunity to work with the National Immunotherapy Coalition and collaborate with a world-class team who share a commitment to reduce cancer incidence and to improve the quality of life of those affected by cancer. Being able to pool resources and agents, we will be able to make a significant leap in developing new immunotherapeutic and combinations that will most benefit patients with various cancer types and stages."

Vivian S. Lee, M.D., Ph.D., M.B.A., University of Utah Senior Vice President for Health Sciences, Dean of the School of Medicine, CEO, University of Utah Health Care: "There really is a no more

fascinating or promising time to be in medicine. The National Immunotherapy Coalition is an amazing opportunity to discuss obstacles that may impede the successful moonshot for cancer and reach the goal of establishing an effective vaccine for this disease in 5 years instead of 20. The University of Utah is deeply committed to solving these dilemmas and I, for one, am heartened that we will help lead the way.”

Andrew M. Evens, DO, MSc, FACP, Professor & Chief, Division of Hematology/Oncology, and Director of the Tufts Cancer Center at Tufts Medical Center: “Tufts Cancer Center is honored to join a group of world-renowned expert physicians, scientists and researchers who have a shared passion for fighting cancer. We understand that cancer can affect every aspect of a person’s life and the lives of their loved ones. That’s why we are dedicated to research focused on helping bring new and innovative treatments to patients in less time.”

Stephen D. Nimer, M.D., Director of the Sylvester Comprehensive Cancer Center and a Professor of Medicine, Biochemistry & Molecular Biology at the University of Miami’s Miller School of Medicine: “Every day, the physicians and scientists within Sylvester Comprehensive Cancer Center’s site disease groups and multidisciplinary research programs, are working to make exciting breakthroughs that can transform the way cancer patients are diagnosed and treated. We look forward to working for the National Immunotherapy Coalition and developing the most innovative strategies to fight the most deadly forms of cancer.”

### **Payers, Providers and Technology Solutions**

Beneficiaries and patients will undergo next-generation molecular sequencing and gain access to over 60 novel and approved molecules to be tested as immunotherapy combinations in 20,000 cancer patients across all tumor types in a master protocol: The QUILT Program.

Daniel J. Hilferty, President and Chief Executive Officer of Independence of Health Group said, “Independence Blue Cross is committed to bringing state-of-the-art advances in oncology care. Although the science is still evolving, experts agree that immunotherapy is a game-changing approach that is expected to revolutionize the way we treat cancer in the future. We are proud to participate in the National Immunotherapy Coalition. We look forward to continued collaboration among this incredible team to develop the most innovative cancer fighting strategy in our lifetime.”

Jim Huffman, Senior Vice President, Head of US Health and Wellness Benefits, Bank of America: “Bank of America provides coverage for about 500,000 employees and their families and for the past five years has worked closely with NantHealth to explore innovative methods for improving health & wellness for their associates. We are doing our part to address an issue that affects the lives of our employees, our customers and clients, and the people in the communities we serve around the world. We are committed to providing the most advanced cancer care to our employees and the National Immunotherapy Coalition with its national footprint of oncologists practicing cutting edge medicine is a valuable resource we will now be able to offer to our 500,000 beneficiaries. Bank of America has partnered with Dr. Soon-Shiong

and his team over the past five years to bring advanced health and wellness to our associates and their families, and we are proud to be a part of this Cancer MoonShot 2020.”

Paul M. Black, Allscripts, Chief Executive Officer & Director: “The National Immunotherapy Coalition is an exciting step towards a more efficient future in cancer treatment, partnering research and health information technology in an entirely new way. As a leader in healthcare information technology solutions, the EHR solution for the NIH and the NCI, we will play the critical role of connecting this newfound medical insight to the communities of healthcare professionals at the frontlines of care delivery. Combining the cutting edge research being done by NantWorks with the power of their Allscripts clinical information solutions will better harness the enormous volume of newly available data, allowing the dissemination of new discoveries much more rapidly to connected communities than has been possible in the past. We have seen already that when new research is presented in the clinicians' workflow efficiently and in a way that feels natural to them, it allows them to focus first and foremost on the well-being of all those dealing with cancer.”

John Chen, Blackberry CEO: "At Blackberry, we understand the value that lies at the intersection of healthcare and technology, which is why we are constantly making advancements to reflect the ever-changing healthcare landscape. As we already power many of the tools that clinicians rely on heavily, we are confident that our involvement in the National Immunotherapy Coalition will be an asset to the future of Cancer treatment. This unique collaboration is pioneering extraordinary solutions to cancer care and we are truly honored to be a part of it.”

### **December 1<sup>st</sup> Meeting of the National Immunotherapy Coalition in Washington DC**

The ambitious goals of the Cancer MoonShot 2020 Program were presented at a meeting hosted by Vice President Joseph Biden at his Naval Observatory residence in Washington DC on December 1, 2015, where members of the coalition presented their shared vision for translating the promise of precision medicine through the delivery of combination immunotherapy to routine clinical cancer care, as well as their shared commitment to accelerate the development of immunotherapy and vaccine therapy as the next generation evolution of cancer care.

Attendees of that meeting, convened and chaired by Dr. Soon-Shiong, included leadership from the pharmaceutical industry representing large pharma and biotech, leadership from national payers including Independence Blue Cross and Bank of America and healthcare leaders from security and interoperability organizations including Allscripts and Blackberry. Major academic cancer centers represented at this meeting included center directors from Massachusetts General Hospital, Johns Hopkins University, University of Miami, University of Utah, Tufts Cancer Center and the John P Murtha Cancer Center at Walter Reed as well as representatives from the oncologists in the community.



### **About The National Immunotherapy Coalition**

The National Immunotherapy Coalition (NIC) is an historic alliance formed through the efforts of top leaders from large pharmaceutical, biotechnology, health insurance and technology companies. The coalition's singular focus is to accelerate the potential of combination immunotherapies as the next generation standard of care in patients with cancer. For more information, please visit <http://www.CancerMoonShot2020.org>

### **About The Cancer MoonShot 2020 Program**

The Cancer MoonShot 2020 Program is the nation's most comprehensive cancer collaborative initiative seeking to accelerate the potential of combination immunotherapy as the next generation standard of care in cancer patients. This initiative aims to explore a new paradigm in cancer care by initiating randomized Phase II trials in patients at all stages of disease in 20 tumor types in 20,000 patients within the next 36 months. These findings will inform Phase III trials and the aspirational moonshot to develop an effective vaccine-based immunotherapy to combat cancer by 2020. For more information, please visit <http://www.CancerMoonShot2020.org>

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# **Exhibit 23**

# **Exhibit 23**

## FEATURE

## Cancer moonshot countdown

Douglas Lowy, Dinah Singer, Ron DePinho, Gregory C Simon &amp; Patrick Soon-Shiong

*Nature Biotechnology* asks representatives from three different cancer ‘moonshot’ initiatives to outline their visions.

Reaching for the moon is not likely to succeed in a single attempt. That is why the United States has witnessed the launch of several different ‘moonshot’ initiatives aiming to galvanize efforts in cancer prevention, diagnosis and treatment. In January, the US government announced the National Cancer Moonshot Initiative. According to the project’s leader, Vice President Joe Biden, whose son Beau’s death from brain cancer last year prompted him to champion the effort, it “is poised to be a critical part of our nation’s anticancer strategy.” The same month, the Cancer MoonShot 2020 Program was officially launched by biotech billionaire Patrick Soon-Shiong to bring together stakeholders from industry, academia, community oncologists and government to produce vaccine-based immunotherapies against cancer. These moonshots joined Texas cancer center MD Anderson’s ambitious Moon Shots Program, which was launched in 2012. *Nature Biotechnology* approached representatives from each of the different initiatives to understand the different aims and strategies being employed.

**What is the specific aim of your moonshot in cancer?**

**Ron DePinho:** The aim of the MD Anderson Moon Shots Program is to more rapidly and systematically convert existing and emerging scientific knowledge into true clinical advancements that will alleviate pain, suffering and death from cancer. Our program brings together large, multidisciplinary teams of researchers, clinicians,

*Douglas Lowy and Dinah Singer are in the Division of Cancer Biology, National Cancer Institute, Bethesda, Maryland, USA. Ron DePinho is in the Department of Cancer Biology, University of Texas MD Anderson Cancer Center, Houston, Texas, USA. Gregory C. Simon is at the White House Cancer Task Force, Washington, DC. Patrick Soon-Shiong is at NantWorks LLC, Culver City, California, USA.*



US vice president Biden has been on a fact-finding tour of laboratories and institutions around the US as he seeks to lead the National Cancer Moonshot. Vice President Joe Biden speaks with Nobel laureate Paul Modrich, left, as Vickers Burdett, wife of Modrich, middle, and A. Eugene Washington, Chancellor for Health Affairs at Duke University, right, listen in a laboratory at Duke University School of Medicine in Durham, North Carolina, on Wednesday, February 10, 2016. Vice President Biden visited Duke to speak about his Cancer Moonshot initiative. (AP Photo/Ben McKeown)

policy experts, educators and staff to mount comprehensive, goal-oriented programs focused on delivering marked improvements in prevention, early detection and treatment options in 12 major cancers: acute myeloid leukemia, myelodysplastic syndrome, chronic lymphocytic leukemia, melanoma, lung cancer, prostate cancer, triple-negative breast cancer, high-grade serous



Ron DePinho

ovarian cancers, B-cell lymphoma, colorectal cancer, glioblastoma, high-risk multiple myeloma, HPV [human papillomavirus]-related cancers and pancreatic cancer.

These moon shots are supported by execution-oriented

implementation platforms, which include seasoned drug development professionals from industry and cancer control experts with government and policy experience. Combining such expertise with that of our academic scholars is probably the most unique aspect of our initiative. Historically, academia’s strength has been its discovery of new knowledge, but it has been less well structured to systematically convert such knowledge into practical endpoints such as new drugs or legislative policy. Effective translation is not only about discovery but also application of knowledge. Translational research is also an inconsistently funded research phase that exists between scientific discovery (largely funded by federal grants) and late-stage clinical trials (financed by the private sector) where ideas often die before they have a chance to be thoroughly tested. Improving the efficiency of preclinical

research and early clinical trials and cultivating the exchange of knowledge back and forth between lab and clinic are essential to successfully traversing this valley of death.



Greg Simon

**Greg Simon:** The goal of the Cancer Moonshot is to make a decade of progress in preventing, diagnosing and treating cancer in five years, ultimately striving to end cancer as we know it. We are taking a critical look at

the entire system of scientific research and medical care and figuring out ways for realigning the incentives of this system to promote breakthrough progress in preventing and treating cancer; creating a new paradigm of generating, sharing and integrating data to enhance patient care; and accelerating the process of bringing new prevention strategies, diagnostics and therapies to patients in communities across the world.

**Patrick Soon-Shiong:** Cancer MoonShot 2020 has several interrelated aims: first, to gain insight into the heterogeneous nature of the cancer cell through the most comprehensive molecular analysis, from the genome to the transcriptome to the proteome and immunome; second, with this insight, to overcome cancer's



Patrick Soon-Shiong

ability to avoid the immune system; third, to use combination immunotherapy to activate the entire immune biological armamentarium, from innate to adaptive immunity, against the cancer; fourth, to deliver all this in near real time for cancer patient care by building a cloud-based, interoperable clinical learning system and a global precision-medicine network of community oncologists and pediatricians; and finally, to accelerate the development of molecular imaging and diagnostic tests combining whole-genome and RNA sequencing with targeted proteomics as well as combination immunotherapy and drug development, all within a decade to five years.

Ultimately, the aim is to win the war on cancer—to get to a point in the very near future when we are managing cancer the same way we might manage any chronic disease, such as diabetes or asthma.

## What are the milestones for your projects?

**DePinho:** Our overarching goal is to more rapidly and dramatically reduce mortality and suffering in cancer, aiming for every patient to contribute to, and potentially benefit from, our efforts. Each moon shot has individual goal-oriented milestones that are evaluated on a semiannual basis to discuss progress and explore additional points of collaboration. In the long term, collaboration among moon shots, platforms, basic scientists and clinicians will increase understanding of the molecular details of cancer, drive new treatments and accelerate cures.

There have already been achievements. Just in immuno-oncology alone, we have launched about 125 clinical trials. By late 2015, our effort had also established a secure database containing clinical information for more than 230,000 patients treated at MD Anderson since 2012, along with full integration of genomic, proteomic and immune profiling data from those patients involved in moon shot research studies.

There is a lot of discipline in the way we structured the program, a high level of accountability and a strong focus on milestones that in the beginning are interim for impact on the cancer problem. To give a specific example: in our cancer control platform, where we focus on things like policy and K-12 education, one milestone we had was that in a given year, we were going to work with many groups to reach stakeholders and legislatures across five different states, to try to educate the public and policy makers about the impact of laws that prevent children under the age of 18 from accessing tanning beds. This effort allowed the MD Anderson Melanoma Moon Shot team and the cancer control platform to provide Texas lawmakers with science-based data that resulted in a state-wide ban on minors' use of tanning beds. Texas was the fourth state to adopt this legislation in 2013, and, today, 14 states have passed the same restriction.

**Simon:** President Obama established the Cancer Moonshot Task Force to coordinate expertise across 20 agencies, sub-agencies and White House offices, as well as to serve as a catalyst for stimulating further private sector advances. This group has been hard at work, with new programs, policies and initiatives being developed and implemented at an accelerated pace. Milestones will include the launch of a series of efforts focused on the spectrum of cancer research and care throughout this year and a report delivered to the President by

December 31 outlining the roadmap for building upon this foundation.

**Soon-Shiong:** Our first milestone is to test 100,000 patients using the 'GPS Cancer' test, which was launched by my company NantHealth (Culver City, California) in January. GPS Cancer is the first CLIA-certified, comprehensive multiomic-based test that integrates sequencing of the whole genome, transcriptomics and targeted proteomics with predictive analytics, resulting in a comprehensive molecular profile of a patient's cancer, which can then inform personalized treatment options. Coverage for the GPS Cancer test has been made available to eligible members of Independence Blue Cross commercial plans since the beginning of March.

Next, 20,000 of these test patients will be matched up and enrolled with an appropriate phase 2 immunotherapy clinical trials in over 20 tumor types, including breast, lung, prostate, ovarian, brain, head and neck, and multiple myeloma. Overall, more than 60 novel immunotherapy and targeted-therapy agents have been made available by pharmaceutical and biotech partners of 2020 for these tests. The governing master trial protocol, called the QUILT Program (Quantitative Integrative Lifelong Trial), is designed to harness and orchestrate all the elements of the immune system (including dendritic cell, T-cell and natural killer (NK) cell therapies) by testing novel combinations of vaccines, cell-based immunotherapy, metronomic chemotherapy, low-dose radiotherapy and immunomodulators and checkpoint inhibitors in molecular-typed patients, with the goal of achieving durable, long-lasting remission for patients with cancer.

A final milestone of our MoonShot is that the findings from QUILT will inform phase 3 trials that ultimately result in the creation of an effective vaccine-based immunotherapy to combat cancer by 2020.

## What specific approaches and technologies are you adopting?

**DePinho:** Our moon shots are supported by ten 'implementation' platforms focused on driving actionable knowledge into clinical endpoints by assembling leading-edge expertise and technology infrastructure in four major areas: data generation (via a cancer genomics laboratory (CGL) platform, an immune checkpoint therapy group and a translational center (CCGT) for discovering and developing targeted therapeutics); product development (via expertise in the

development of small molecules (IACS), biologics (ORBIT) or adoptive cell therapies); data integration analysis (via advanced analytic platforms for clinical decision-making and an institutional longitudinal patient disease registry); and finally, a cancer prevention and control effort.

As I mentioned, we now have profiles for over 230,000 MD Anderson patients that combine clinical information with tumor 'omic' and immune monitoring data. Over time, additional research data will be added. This 'learning system' will provide unprecedented, controlled access for MD Anderson researchers to generate hypotheses and make connections between tumor characteristics, as detailed from molecular analysis, test results, imaging and other sources, and the efficacy of treatment. Our big data warehouse is designed ultimately to accept and share data from external sources as well.

**Simon:** Under the Cancer Moonshot, we are working to apply 21<sup>st</sup> century technology to transform knowledge and data into real solutions for patients. For example, we are working to apply the nation's most powerful computational capabilities to analyze vast and complex datasets to make sense about which treatments work for which patients. We are also focused on bringing together the numerous stakeholders to incentivize new ways of stimulating action and fostering collaborations, which will be key to the success of this effort.

Investments from the National Cancer Moonshot Initiative will support cutting-edge research opportunities. These include cancer vaccine development, technologies for the development of diagnostics for early cancer detection, immunotherapies and combination therapies for an expanded range of cancers, genomic profiling of primary tumors and their surrounding cells, technologies for facilitating data sharing, and programs for targeting pediatric cancers. An Oncology Center of Excellence [will run] under the auspices of the US Food and Drug Administration (FDA) to leverage the combined the combined skills of regulatory scientists and reviewers with expertise in drugs, biologic and devices. Finally, under the umbrella of the initiative, a Vice President's Exceptional Opportunities in Cancer Research Fund is planned to provide financing to scientists, cancer physicians, philanthropic organizations, and pharma and biotech companies working together on major new innovations in the understanding of, and treatment for, cancer.

**Soon-Shiong:** As I mentioned, there will be detailed molecular characterization of the

patient's tumor and immune status via diagnostic testing. This will be synergized with all the therapeutic tools at our disposal—from standard chemotherapy, to radiotherapy, to targeted therapy, to monoclonal antibody therapy, to cell-based immune therapy, to chemokines and cytokine therapy, to approved drugs and to drugs in development.

With these tools in place, we can establish a real-world, rapid clinical learning system to understand how we could optimize this maze of combination therapy. This will require health information technology and next-generation interoperable software. NantHealth's clinical-decision support software provides evidence-based treatment support, which may include QUILT trial identification based on genomic and proteomic sequencing results. The company's provider portal technologies will also allow oncologists and other clinicians to check patient eligibility for sequencing, request health plan authorization, and monitor and view test results, while helping to coordinate the patient's care across the care continuum.

#### How are these efforts being funded?

**DePinho:** We have mobilized more than \$600 million over the past couple of years for these projects, with nearly \$350 million in private philanthropic commitments. These philanthropic funds are complemented by several hundred million dollars raised through grants from the US National Institutes of Health (Bethesda, MD) and the Cancer Prevention & Research Institute of Texas and contracts as well as by returns from IP [intellectual property], which are plowed back into our mission to end cancer. MD Anderson ranks number one in the nation in IP-related commercialization revenues as well as corporate alliance revenue, outpacing all universities in the country.

**Simon:** The administration is launching the National Cancer Moonshot with \$1 billion in funding. Information can be found at <https://www.whitehouse.gov/the-press-office/2016/02/01/fact-sheet-investing-national-cancer-moonshot>. Funding will include \$195 million in new cancer activities at the National Institutes of Health (NIH) in fiscal year 2016. In fiscal year 2017, the Administration's budget will propose to continue this initiative with \$755 million in mandatory funds for new cancer-related research activities at both NIH and the FDA. The Departments of Defense and the Veterans Affairs are also increasing their investments in cancer research, including the funding of Centers of Excellence focused on specific

cancers and conducting large longitudinal studies to help determine cancer risk factors and enhance treatment.

**Soon-Shiong:** Thus far, large biopharmaceutical companies have taken the lead to support the efforts. Specifically, Amgen (Thousand Oaks, California), Celgene (Summit, New Jersey) and my ecosystem of companies forming NantWorks have committed to this effort. NantWorks will shortly announce the funds that it has raised in support of the goals of Cancer MoonShot 2020, and it is expected that the amount will exceed a billion dollars. In addition, Independence Blue Cross and self-insured payers, such as Bank of America (New York), have committed to fund the GPS screening test needed.

Finally, the NantHealth Foundation and the Chan Soon-Shiong Institute of Molecular Medicine at Oxford University, UK, a 501c3 medical research organization, has been formed and will commit a billion dollars to support cancer centers around the nation and community oncologists to make available the treatments and trials of the initiative.

The funding needed to win the war on cancer should be considered in the context of that needed to place a man on the moon or the successful NASA Space shuttle program with its multiple launches. To sufficiently fund this initiative, combined support is needed from philanthropy, the private sector, government agencies and even NGOs [nongovernmental organizations].

#### Who are the main stakeholders?

**DePinho:** The Moon Shots Program has brought together nearly 2,000 faculty and staff out of 21,000 employees at MD Anderson. It's a significant effort involving basic scientists, oncologists, surgeons, radiologists, physician-scientists, experts in data management and analysis, cancer prevention and control, and other disciplines in 12 different cancers.

Using immunotherapy as an example, we've signed research collaborations with a dozen companies, including multinational pharma companies like Pfizer (New York), Bristol-Myers Squibb (Princeton, NJ), GlaxoSmithKline (London), Johnson & Johnson (New Brunswick, NJ) and MedImmune (part of London-based AstraZeneca) and biotech companies like Intrexon (Germantown, MD), Ziopharm (Boston), Kymab (Oxford, UK), Astellas Pharma (Tokyo), CytomX Therapeutics (S. San Francisco, CA), Jiangsu Hengrui Medicine (Shanghai) and AbbVie Biotherapeutics (Redwood City, CA)—not only to conduct



clinical trials for their experimental drugs, but also to bring our scientists and theirs together to compare notes on research and design preclinical studies and new clinical trials to improve treatment. As always, we collaborate in clinical trials with other cancer centers testing new immunotherapies, with several thousand patients involved in more than 165 such trials now open at MD Anderson.

In cancer prevention and control, we work closely with advocacy groups, like the CATCH Foundation and Tobacco-Free Kids, and our governmental relations colleagues to educate legislators. In addition, we have extensive interactions with governmental agencies such as the CDC [US Centers for Disease Control and Prevention] (Atlanta) and have engaged in strategic public health discussions with other governments, including China, Portugal and Mexico.

**Simon:** The Vice President is issuing the call far and wide, recognizing that innovative solutions to tough problems often arise from unlikely sources or the combination of seemingly disparate expertise. Thus, the Cancer Moonshot aims to break down conventional silos and bring together patient advocates, health care providers, biomedical researchers, technological innovators, industry leaders and more to serve the ultimate Cancer Moonshot stakeholder: the patient.

**Dinah Singer:** Readers can find members of the Task Force and of the Blue Ribbon Panel at their respective websites (<https://www.whitehouse.gov/the-press-office/2016/01/28/memorandum-white-house-cancer-moonshot-task-force> and <http://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel>). The 28-member Blue Ribbon Panel represents a spectrum of scientific areas, including biology, immunology, genomics, diagnostics, bioinformatics, and cancer prevention and treatment. Scientific members also include investigators with expertise in clinical trials and cancer health disparities. Importantly, the members



Dinah Singer

of cancer advocacy groups and pharmaceutical and biotechnology companies will be represented on the panel and its working groups. The Panel has announced seven working groups, involving 10 to 12 leading experts per group. The working groups are tasked

with helping the Panel develop two to three recommendations for major research opportunities that could lead to significant breakthroughs.

Community input will be critical to success and members of the scientific community and general public are encouraged to submit ideas for advancing progress against cancer in one or more areas on the Cancer Research Ideas platform here: <https://cancerresearchideas.cancer.gov/a/pages/about>.

**Soon-Shiong:** We have nearly 150 leaders from a diverse community across pharma, biotech, technology, academic and community oncology, the US National Cancer Institute (NCI) and not-for-profit thought leaders.

Industry partners include companies from the pharmaceutical and biotech sector and from communications technology. For the former, participants include Celgene, Amgen, NantWorks, NantKwest (San Diego), Etubics (Seattle), Altior Bioscience (Miramar, Florida) and Precision Biologics (Westlake Village, California). In communications technology, we have brought on board such leaders as Allscripts (Chicago) CEO, Paul Black and BlackBerry (Waterloo, Ontario, Canada) CEO John Chen.

Major participating academic cancer centers include Johns Hopkins (Baltimore), Tufts University (Boston) and Columbia University (New York); community hospital and ambulatory settings are also contributing under the Precision Medicine Global Network, which includes nearly 1,000 oncologists in the United States.

We also have as partners leading insurance companies, such as Independence Blue Cross CEO Daniel Hilferty and Bank of America's (New York) Head of US Health and Wellness Benefits Jim Huffman, who have committed to support payment for our diagnostic tests. The NCI also is playing a direct role. The US-wide master protocol will be designed under CRADA agreements between companies and the NCI, with scientific guidance provided by the NCI's branch chiefs of Tumor Immunology and Biology Laboratory and Medical Oncology using the recently published US Food and Drug Administration guidance on 'Co-development of two or more new investigational drugs for use in combination'.

#### Are you concerned about confusion on the different cancer moonshots?

**DePinho:** In the first three years of our Moon Shots Program, we've had early successes and accomplished great strides, and there's so

much more ahead of us in this golden era of cancer research. I had the privilege of speaking several times with Vice President Biden over the past few years about our program and how we organized our efforts. The newly announced national moon shot, under the leadership of the Vice President, will only further stimulate collaboration and achievement in our nation's fight to end cancer. We also are pleased to have two of our best cancer scholars—Jim Allison and Al Yung—on the Blue Ribbon Panel to advise the NCI in its work with Vice President Biden. We all plan to work together for our patients.

**Simon:** The purpose of the Cancer Moonshot is to inspire the people all around the world to rise to the charge from the President. Any effort focused on accelerating preventing, diagnosing and treating this terrible disease is a win.

**Douglas Lowy:** The Vice President's enthusiasm is welcomed by the community of researchers, health professionals and patients who share his passion and belief that great things are possible by accelerating cancer research with leadership and resources. We are committed to



Douglas Lowy

breaking down silos and stimulating the groundbreaking work already underway. To be successful, we must hear a broad range of perspectives to take full advantage of the exceptional current opportunities in cancer research.

**Soon-Shiong:** No, not concerned at all. These moonshots are mutually reinforcing and ultimately share the same goals—to win the war on cancer. The Cancer MoonShot 2020 program has been my vision for over a decade, culminating in its 'liftoff' in January 2016. Our initiative has a laser focus on patients with active disease and to accelerate combination immunotherapy and big data integration in near real time. It is a highly focused effort that specifically looks at the potential of combination immunotherapy as the next standard of care for cancer patients, by leveraging insights from DNA and RNA sequencing with quantitative proteomics. It is led by the private sector and brings together pharma, biotech, payers, academia and community oncologists for the aspirational goal of developing a cancer vaccine by 2020.